

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/26993> holds various files of this Leiden University dissertation

**Author:** Stam, Anine

**Title:** Genetics of migraine and related syndromes

**Issue Date:** 2014-06-26

# **GENETICS OF MIGRAINE AND RELATED SYNDROMES**

Anine Stam

---

Anine Henrike Stam

Genetics of migraine and related syndromes

PhD Thesis, Leiden University Medical Center, Leiden,  
2014

ISBN: 978-90-9028280-0

Layout and printed by: Off Page

© A.H. Stam, 2014

Copyright of published material in chapters 2-8, 11 and  
12 lies with the publisher of the journal listed at the  
beginning of each chapter. No part of this thesis may be  
reproduced in any form, by print, photocopy, digital file,  
internet, or any other means without written permission  
of the copyright holder.

---

# GENETICS OF MIGRAINE AND RELATED SYNDROMES

Proefschrift

ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus prof.mr. C.J.J.M. Stolker,  
volgens besluit van het College voor Promoties  
te verdedigen op donderdag 26 juni 2014  
klokke 16:15 uur

door

Anine Henrike Stam

geboren te Den Helder in 1979

**Promotiecommissie**

**Promotores**

Prof.dr. M.D. Ferrari

Prof.dr. A.M.J.M. van den Maagdenberg

**Co-promotor**

Dr. G.M. Terwindt

**Overige leden**

Prof.dr. R.A.C. Roos

Emeritus prof.dr. R.R. Frants

Dr. J. Haan

Prof.dr. C.M. van Duijn (Erasmus MC, Rotterdam)

The studies presented in this thesis were performed at the Department of Neurology and Human Genetics of Leiden University Medical Center (LUMC). This work was supported by grants of the Netherlands Organization for Scientific Research (NWO) (907-00-217, and Vidi 917-11-318, GMT, 920-03-473, AHS, Vici 918-56-602 and Spinoza 2009, MDF), the Center of Medical Systems Biology (CMSB) 050-060-409 and the European Union Seventh Framework programme NIMBL 241779.

Financial support for publication of this thesis has been provided by de Nederlandse Hoofdpijn Vereniging.

## CONTENTS

Chapter 1	General introduction & scope of the thesis	9
PART I A MONOGENIC MIGRAINE SYNDROME: FHM		31
Chapter 2	CACNA1A R1347Q: a frequent recurrent mutation in hemiplegic migraine <i>Clinical Genetics 2008;74:481-5</i>	33
Chapter 3	CACNA1A mutation linking hemiplegic migraine and alternating hemiplegia of childhood <i>Cephalgia 2008;28:887-91</i>	43
Chapter 4	Early seizures and cerebral edema after trivial head trauma associated with the CACNA1A S218L mutation <i>Journal of Neurology Neurosurgery and Psychiatry 2009;80:1125-9</i>	53
Chapter 5	Familial hemiplegic migraine is associated with febrile seizures in an FHM2 family with a novel de novo ATP1A2 mutation <i>Epilepsia 2009;50:2503-4</i>	67
Chapter 6	First mutation in the voltage-gated Na <sub>v</sub> 1.1 subunit gene SCN1A with co-occurring familial hemiplegic migraine and epilepsy <i>Cephalgia 2009;29:308-13</i>	75
Chapter 7	Episodic ataxia associated with EAAT1 mutation C186S affecting glutamate reuptake <i>Archives of Neurology 2009;66:97-101</i>	87
PART II A MONOGENIC MIGRAINE ASSOCIATED SYNDROME: RVCL/CHARIOT		97
Chapter 8	C-terminal truncations in human 3'-5' DNA exonuclease TREX1 cause autosomal dominant retinal vasculopathy with cerebral leukodystrophy <i>Nature Genetics 2007;38:1068-70</i>	99
Chapter 9	The clinicopathologic spectrum of Cerebral Hereditary Angiopathy with vascular Retinopathy and Impaired Organ function caused by TREX1 mutations (CHARIOT). A review of 78 mutation carriers from 11 unrelated families <i>Submitted</i>	115

---

Chapter 10	Cerebral hereditary angiopathies RVCL and CADASIL display distinct impaired vascular functionality <i>Work in progress</i>	137
PART III	MIGRAINE AND COMORBIDITY IN A GENETIC ISOLATE	161
Chapter 11	Shared genetic factors in migraine and depression: evidence from a genetic isolate <i>Neurology 2010;74:288-94</i>	163
Chapter 12	Migraine is not associated with enhanced atherosclerosis <i>Cephalalgia 2013;33:228-35</i>	177
Chapter 13	General discussion	191
Addendum	Summary	213
	Nederlandse samenvatting	217
	List of abbreviations	221
	List of publications	223
	Curriculum vitae	227



